

Executive Summary for *Imitrex*

This response may include reference to information about Imitrex® (sumatriptan succinate) Injection; Imitrex® (sumatriptan succinate) Tablets; Imitrex® (sumatriptan) Nasal Spray.

- Important safety information is found in the attached Prescribing Information.
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BACKGROUND INFORMATION

Migraine is a highly disabling neurobiological disease affecting 28 million Americans, which is equivalent to 13% of the U.S. population. Migraine is a treatable disease and therapeutic options have improved over the last 10 years, however the burden of migraine in the U.S. remains substantial and migraine remains underdiagnosed and under-treated in the U.S. ^{(1) (2)}

Advances over the last 10 years have brought forth migraine specific prescription medications that treat the pain and associated symptoms of migraine without causing sedation. More effective treatments not only improve clinical care of migraine, but decrease the cost by reducing the utilization of the health-care system and the use of concomitant medications.

Imitrex, the most widely studied migraine medication on the market, is the only 5HT_{1B/1D} agonist available in three formulations: injection, nasal spray, and tablets. The multiple formulations of *Imitrex* offer the opportunity to utilize the stratified care approach recommended by the US Headache Consortium Guidelines, with the same molecular entity. ⁽³⁾

EFFICACY AND SAFETY OF *IMITREX* FOR MIGRAINE

Time to Onset of Efficacy

During the pivotal clinical trials, onset of relief began as early as 10 minutes after single doses of *Imitrex* Injection and as early as 15 minutes after single doses of *Imitrex* Nasal Spray 20 mg. ^{(4) (5) (6) (7)} Onset of relief occurs as early as 20 minutes with *Imitrex* Tablets 100 mg and 30 minutes with 50 mg. ⁽⁸⁾

Efficacy and Safety of *Imitrex* Injection

During controlled trials with *Imitrex* Injection, 81-82% of patients treated with a 6-mg dose experienced headache relief 2 hours following treatment. ⁽⁹⁾ Some of the most common adverse events reported during controlled clinical trials were injection site reactions (mild and transient stinging, redness, or swelling), tingling, dizziness/vertigo, and warm/hot sensations. ⁽¹⁰⁾

As of February 2006, *Imitrex* Injection has been formulated to allow a patient to self-administer a 4 mg dose via the *Imitrex* STATdose System®. The *Imitrex* STATdose System is a compact, easy to use, and simple delivery device for the subcutaneous (SC) administration of either the 4 mg or 6 mg dose of *Imitrex*.

Efficacy and Safety of *Imitrex* Nasal Spray

During controlled trials with *Imitrex* Nasal Spray, 45-49% and 55-64% of patients treated with either 5 mg or 20 mg, experienced headache relief 2 hours following treatment, respectively. ⁽¹¹⁾ The most common adverse event was disturbance of taste, which was reported by 14-25% of patients. ⁽¹¹⁾

Efficacy and Safety of *Imitrex* Tablets

As of January 2004, *Imitrex* Tablets have been reformulated as a rapid release tablet and have replaced the conventional *Imitrex* tablet. The reformulated tablets still contain the same active ingredient, sumatriptan succinate. With the reformulated tablet, nearly 100% of sumatriptan is dispersed within 2 minutes compared to less than 20% with the conventional tablet. ⁽¹²⁾

The reformulated *Imitrex* Tablets are bioequivalent to the conventional *Imitrex* tablet as measured by the entire area under the curve (AUC_{0-infinity}) and maximum concentration (C_{max}). However, early exposure measures with the reformulated tablets, such as AUC₀₋₂ and time to maximum concentration (T_{max}), showed improvement when compared with the conventional *Imitrex* tablet. The reformulated tablets reach T_{max} 10-15 minutes earlier than the conventional *Imitrex* tablet. ⁽¹²⁾

Efficacy of Reformulated *Imitrex* Tablets for Treatment of Migraine at Mild Pain

Neurobiological research indicates that the intracranial nociceptors respond to the pain of migraine in stages. ^{(13) (14)} If pain can be stopped early, before sensitization occurs, the cascade of pain responses common to acute migraine may be controlled. Data from retrospective and prospective analyses suggest that for improved efficacy, *Imitrex* Tablets should be administered at the first sign of pain, or at the mild pain phase of a migraine attack. ^{(15) (16) (17)}

In a multi-center, randomized, double-blind, placebo-controlled single attack study, a pain-free response was observed as early as 30 minutes with reformulated *Imitrex* Tablets 100 mg, treating during the mild pain phase of the migraine attack. ⁽¹⁸⁾ It demonstrated that 66% and 51% of patients treated with 100 mg and 50 mg of reformulated *Imitrex* were pain-free at 2 hours. In the per protocol population (population that complied with protocol), 75% and 53% of patients treated with 100 mg and 50 mg of reformulated *Imitrex* at the first sign of mild pain were pain-free at 2 hours. A pain-free dose response was observed with the 100-mg dose producing the highest pain-free results. *Imitrex* Tablets were generally well tolerated.

ECONOMIC AND HEALTH OUTCOMES

Economic

Delaying treatment until the late phase of headache may require more intensive or multiple treatment interventions. ⁽¹⁹⁾ Early intervention treatment strategies may result in cost advantages, as migraineurs achieve higher efficacy and use fewer doses for each attack. In a study by Cady, the costs per pain-free migraine attack with both *Imitrex* 50 mg and 100 mg were greatly reduced when patients treated their migraine at the onset of mild pain, with the 100 mg performing better than the 50 mg. ⁽¹⁹⁾ In addition, overall consumption of the number of tablets needed to treat an attack was reduced.

Health Outcomes

Health Outcome studies have demonstrated the positive benefits of *Imitrex* to patients, providers, payers, and employers. Studies have shown that *Imitrex* improves patient-reported health-related quality of life (HRQOL), and patient satisfaction with their migraine therapy. ^{(20) (21)}

⁽²²⁾ Workplace productivity studies have demonstrated the positive impact of *Imitrex* on reducing lost productivity and allowing patients to

rapidly return to non-workplace productivity. (22) (23) (24) (25) Additionally, *Imitrex* has been shown to decrease health care resource utilization consumption.

PATIENT EDUCATION

Migraine Matrix® is a disease state management program developed by GlaxoSmithKline which provides patient education and physician diagnostic and educational tools to assist in the appropriate management of migraine patients. Migraine Matrix® is designed to enhance clinical decision making through the use of educational materials and to encourage consistency and continuity of migraine care. Migraine Matrix® tools are not designed to support the prescribing of one particular agent.

SUMMARY

Migraine is a treatable disease and therapeutic options have improved over the last 10 years. The vast clinical experience and multiple formulations of *Imitrex* offer the flexibility to utilize a stratified care approach with proven efficacy and safety. Furthermore, *Imitrex* when used early in the migraine attack may result in cost advantages, as migraineurs achieve higher efficacy and use fewer doses for each attack.

Enclosure: Prescribing Information for *Imitrex* Tablets

Enclosure: Prescribing Information for *Imitrex* Injection

Enclosure: Prescribing Information for *Imitrex* Nasal Spray

Some information contained in this response may not be included in the approved Prescribing Information. This response is not intended to offer recommendations for administering this product in a manner inconsistent with its approved labeling.

In order for GlaxoSmithKline to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 888-825-5249. Please consult the attached Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

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